CLAIMS

1. A peptide that is a maturation product of the Basic Prolin-rich Lacrimal Protein (BPLP) or a peptide derivative of said maturation product, wherein the peptide or peptide derivative exhibits a modulatory, especially an inhibitory property against a metallo-ectopeptidase.

2. The peptide of claim 1, wherein said metallo-ectopeptidase is NEP or APN.

3. The peptide or peptide derivative of claim 1, wherein said peptide or peptide derivative comprises the sequence X1-X2-Arg-Phe-Ser-Arg, wherein :

- X1 represents H atom or a Tyr amino acid or a Cys amino acid,
- X2 represents Gln or Glp when X1 is H, or X2 represents Gln when X1 is Tyr,

wherein said sequence X1-X2-Arg-Phe-Ser-arg is the C-terminal part of said peptide.

4. The peptide of claim 1, that consists of sequence X1-X2-Arg-Phe-Ser-Arg.

5. The peptide of claim 3, wherein the said peptide comprises the sequence QRFSR, YQRFSR, or CQRFSR.

6. The peptide of claim 5, which consists of sequence QRFSR.

7. The peptide of claim 5, which consists of sequence YQRFSR.

8. The peptide of claim 5, which consists of sequence CQRFSR.

9. A nucleic acid that encodes a peptide of any of claims 1 to 8.

10. A vector for cloning and/or expression, which vector comprises a nucleic acid of claim 9.

11. A host cell comprising the nucleic acid of claim 9 or the vector of claim 10.

12. An antibody that specifically recognizes a peptide of any of claims 1 to 8.

13. An antibody that specifically recognizes the BPLP protein.

14. A pharmaceutical composition comprising a peptide according to any of claims 1 to 8 or a derivative or a mimetic thereof, in association with a pharmaceutically acceptable carrier.

15. A pharmaceutical composition, comprising a polymer of a peptide according to claims 1 to 8, or a derivative or mimetic thereof, in association with a pharmaceutically acceptable carrier.

16. A pharmaceutical composition comprising a nucleic acid of claim 9 or a vector expressing said nucleic acid.

17. A pharmaceutical composition comprising a nucleic acid coding for the BPLP protein or a vector expressing said nucleic acid.

18. A pharmaceutical composition comprising an antibody of claim 12 or 13.

19. A pharmaceutical composition comprising a BPLP protein in association with a pharmaceutically acceptable carrier.

20. A pharmaceutical composition according to claims 14 to 17 and 19, comprising a second pharmaceutical agent that acts synergistically with BPLP-peptide.

21. Use of a peptide according to any of claims 1 to 8 or a derivative or a mimetic thereof, for the preparation of a medicament for the prevention or treatment of a disease wherein a modulation of the activity of a membrane metallopeptidase is sought.

22. The use of claim 21, wherein the metallopeptidase is a membrane-zinc metallopeptidase.

23. The use of claim 22, wherein the metallopeptidase is NEP or APN.

24. The use of a peptide according to any of claims 1 to 8, or a derivative or a mimetic thereof, for the preparation of a medicament for the prevention or treatment of pain.

25. The use of claim 24, wherein the pain is chronic, acute, visceral inflammatory or neuropathic pain.

26. The use of a peptide according to any of claims 1 to 8, or a derivative or a mimetic thereof, for the preparation of a medicament for the prevention or treatment of hydro-mineral imbalance.

27. The use of claim 26, for the prevention or treatment of bone, teeth, kidney, parathyroid, pancreas, intestine, stomach mucosa, prostate, and salivary gland disorders that are caused by hydro-mineral imbalance.

28. The use of claim 27, wherein the disorder is selected from the group consisting or hyper or hypo-parathyroidism, osteoporosis, pancreatitis, submandibular gland lithiasis, nephrolithiasis and osteodystrophy.

29. The use of a peptide according to any of claims 1 to 8 or a derivative or a mimetic thereof, for the prevention or treatment of impaired interpersonal and behavioural disorder.

30. The use of claim 29, wherein the disorder is selected from the group consisting of avoidance disorder, decreased awareness disorder, autistic disorder, attention deficit hyperactivity disorder, hospitalism, impaired interpersonal functioning and relationship to the external world, schizoid personality disorder, schizophrenia, decreased interest in environment, impaired social activity linked to sexuality, and impaired sexual behaviour.

31. The use of claim 29, wherein the disorder is depressive disorder.

32. The use according to claim 21, for the prevention or treatment of inflammatory arthritis.

33. The use according to claim 21, wherein the peptide or derivative or mimetic thereof acts as a natriuretic agent.

34. The use of a peptide according to claim 21, wherein the peptide acts as a diuretic agent.

35. The use according to claim 21, for the prevention or treatment of atherosclerosis.

36. The use according to claim 21, for the prevention or treatment of a tumor.

37. The use according to claim 21, for the prevention or treatment of inflammatory bowel disease.

38. The use according to claim 21, for the treatment of infections.

39. The use according to claim 21, for controlling immuno-inflammatory responses.

40. The use according to claim 21, for the treatment of a neurodegenerative disease.

41. The use according to claim 40, for the treatment of a neurodegenerative disease associated with amyloidosis.

42. Use of a nucleic acid of claim 9, for the preparation of a medicament for the prevention or treatment of a disease as defined in any of claims 21 to 41.

43. Use of an antibody of claim 12, for the preparation of a medicament for the prevention or treatment of a disease as defined in any of claims 21 to 41.

44. Use of a BPLP protein for the preparation of a medicament for the prevention or treatment of a disease as defined in any of claims 21 to 41.

45. Use of a nucleic acid that encodes a BPLP protein for the preparation of a medicament for the prevention or treatment of a disease as defined in any of claims 21 to 41.

46. Use of an antibody directed against BPLP protein according to claim 13 for the preparation of a medicament for the prevention or treatment of a disease as defined in any of claims 21 to 41.

47. An *in vitro* method for prognosis, diagnosis or determination of the evolution of a condition involving an altered production of BPLP or of any of its maturation products, which method comprises detecting, or quantifying in a biological sample of a test subject, a BPLP protein or a maturation products thereof, and comparing the production of BPLP protein or maturation products with the production of the same in a biological sample of a control subject.

48. The method of claim 47, wherein detection of the production of BPLP or of any of its maturation products is performed by contacting a biological sample with an antibody as defined in claim 12 or 13.

49. An *in vitro* method for prognosis or diagnosis of a condition involving an altered production of BPLP or of any of its maturation products, which method comprises detecting in a biological sample of a test subject, a quantitative and/or qualitative abnormality in the BPLP gene or in its transcript.

50. An *in vitro* method for screening compounds for their ability to bind to the NEP binding site for the BPLP protein or a maturation product thereof, comprising the steps of:

a) incubating a candidate compound with a NEP expressing cell, in the presence of the BPLP protein or a maturation product thereof, or in the presence of any peptide retaining the binding specificity or the physiological activity of BPLP protein or of its maturation products;

b) determining the ability of the candidate compound to compete with the BPLP protein or a maturation product thereof, or with the peptide retaining the binding specificity or the physiological activity of BPLP protein or of its maturation products, for binding to NEP.

51. The method of claim 50, comprising the steps of :

a) preparing a cell culture or preparing an organ specimen or a tissue sample containing NEP binding sites for the BPLP protein or maturation products thereof ;

b) adding the candidate compound to be tested in competition with half-saturation concentration of labeled BPLP protein or maturation product thereof, or the peptide that retains the binding specificity or the physiological activity of the BPLP protein or of its matured products ;

c) incubating the cell culture, organ specimen or tissue sample of step a) in the presence of the candidate compound during a time sufficient and under conditions for the specific binding to take place ;

d) quantifying the label specifically bound to the cell culture, organ specimen or tissue sample in the presence of various concentrations of candidate compound.

52. A process for determining the affinity of a compound that specifically binds to the NEP binding site for the BPLP protein or maturation products thereof, comprising the steps of :

a) preparing a cell culture or preparing an organ specimen or a tissue sample containing NEP binding sites for the BPLP protein or maturation products thereof ;

b) adding the candidate compound which has previously been labeled with a radioactive or a nonradioactive label ;

c) incubating the cell culture, organ specimen or tissue sample of step a) in the presence of the labeled candidate compound during a time sufficient and under conditions for the specific binding to take place ; and

d) quantifying the label specifically bound to the cell culture, organ specimen or tissue sample in the presence of various concentrations of the labeled candidate compound.

53. An *in vitro* method for screening compounds for their ability to act as agonists or antagonists of the BPLP protein or maturation products thereof on NEP activity, which method comprises the steps of :

a) incubating a candidate compound with a NEP expressing cell, in the presence of (i) the BPLP protein or a maturation product thereof, or any peptide retaining the binding specificity or the physiological activity of the BPLP protein or of its matured products, and (ii) a NEP substrate ;

b) determining the endoproteolysis of the NEP substrate by the NEP, wherein an increased endoproteolysis in the presence of the candidate compound, in comparison with the endoproteolysis in the absence of the candidate compound, is indicative of an antagonist activity; while a decreased endoproteolysis in the presence of the candidate compound, in comparison with the endoproteolysis in the absence of the candidate compound, is indicative of an agonist activity.

54. The method of claim 53, for screening a compound that is an agonist of the BPLP protein or a maturation product thereof, comprising the steps of :

a) preparing a cell culture or preparing an organ specimen or a tissue sample containing NEP binding sites for the BPLP protein or a maturation product thereof;

b) incubating the cell culture, organ specimen or tissue sample of step a) at concentrations allowing measurement of NEP enzymatic activity in the presence of (i) the candidate compound, (ii) a half-saturating concentration of the BPLP protein or a maturation product thereof or any peptide retaining the binding specificity or the physiological activity of the BPLP protein or of its matured products and (iii) a NEP substrate, during a time sufficient for the endoproteolysis of the NEP substrate to take place under initial velocity conditions ;

c) quantifying the activity of the NEP present in the biological material of step a) by measuring the levels of NEP substrate endoproteolysis, respectively in the presence or in the absence of the candidate compound and in the presence or in the absence of the BPLP protein or a maturation product thereof, or of the peptide retaining the binding specificity or the physiological activity of the BPLP protein or of its matured products.

55. The method of claim 53 for screening a compound that is an antagonist of the BPLP protein or a maturation product thereof, comprising the steps of :

a) preparing a cell culture or preparing an organ specimen or a tissue sample containing NEP binding sites for the BPLP protein or a maturation product thereof;

b) incubating the cell culture, organ specimen or tissue sample of step a) at concentrations allowing measurement of NEP enzymatic activity under initial velocity conditions in the presence of a submaximal concentration of the BPLP protein or a maturation product thereof or any peptide retaining the binding specificity or the physiological activity of the BPLP protein or of its matured products, and a NEP substrate, in the presence of the candidate compound, during a time sufficient for the endoproteolysis of the NEP substrate to take place under initial velocity conditions ;

c) quantifying the activity of the NEP present in the biological material of step a) by measuring the levels of NEP substrate endoproteolysis, respectively in the presence or in the absence of the candidate compound and in the presence or in the absence of the BPLP protein or a maturation product thereof or of the peptide retaining the binding specificity or the physiological activity of the BPLP protein or of its matured products.

56. A molecular complex comprising :

- a metallo-ectopeptidase receptor, especially a NEP receptor or an APN receptor, binding site of the BPLP-protein or maturation products thereof ;
- the BPLP-protein or maturation products thereof.

57. Use of an agent that modulates the interaction between endogenous BPLP protein or maturation product and a membrane metallopeptidase for the preparation of a therapeutic composition for preventing or treating diseases wherein a modulation of the activity of said membrane metallopeptidase is sought.